UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/694,586	10/27/2003	Ekambar R. Kandimalla	HYB-005US5	3762

7590 05/12/2009

WAYNE A. KEOWN
SUITE 1200
500 WEST CUMMINGS PARK
WOBURN, MA 01801

EXAMINER	
HORNING, MICHELLE S	
ART UNIT	PAPER NUMBER
1648	
MAIL DATE	DELIVERY MODE
05/12/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/694,586	KANDIMALLA ET AL.	
	Examiner	Art Unit	
	MICHELLE HORNING	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20,21 and 41-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20,21 and 41-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is responsive to communication filed 2/26/2009. The status of the claims is as follows: claims 1-19 and 22-40 are cancelled and claims 20-21 and 41-51 are both pending and under current examination.

Any rejection not reiterated herein has been withdrawn. Note that the rejection under 35 USC 103 (Schwartz and Jennings) has been withdrawn due to Examiner's misinterpretation of the art. More specifically, Schwartz discloses using non-naturally occurring sugars (e.g. arabinose) in immunomodulatory compounds; see below for discussion.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/26/2009 has been entered.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 20-21, 42-44, 46-48 and 50-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 6562798 (Schwartz) and Chaix et al (Bioorganic and Medicinal Chemistry Letters, 1996).

Schwartz discloses an immunostimulatory oligonucleotide comprising a CpG dinucleotide wherein the C is modified (see Abstract) and a phosphorothioate (col. 8, lines 56-65). Figure 1 depicts the structure of 5-bromocytosine substituted CpG with the following characteristics: D is a hydrogen donor, D' is a bromide or an electron withdrawing group (col. 4), A is a hydrogen bond acceptor, X is a carbon and S is a pentose. Thus, the structural limitations of a non-natural pyrimidine nucleoside of claims 42-44 and 48 have been met by the prior art. Schwartz also discloses using modified sugars, including the non-naturally occurring arabinose which may be substituted in the immunostimulatory sequence (see col. 8, lines 25-67).

Schwartz does not teach inserting a 3'-3' linker and an immunostimulatory oligonucleotide with two accessible 5' ends.

Chaix teaches using 3'-3' linkages in oligonucleotides (see Abstract). The authors note that "These 3'-3' analogs showed increased resistance against nuclease-mediated degradation compared to the 5'-3' linked oligonucleotides" (see Abstract). Also noted is that using a 3'-3' linkage between two sequences would result in oligonucleotides with two accessible 5' ends; see Table 1, Sequence # 2 (p. 828) which depicts an oligonucleotide comprising a 3'-3' linkage and two accessible 5' ends.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to further include a 3'-3' linker in the immunostimulatory oligonucleotide taught by Schwartz because such a linker results in an increased resistance again nuclease-mediated degradation.

Response to Arguments

Applicant's arguments filed 12/4/2008 have been fully considered but they are not persuasive. Applicant contends that part of the invention was the recognition that immunostimulatory activity requires an accessible 5' end, but not an accessible 3' end and that Applicants' invention teaches that making the 3' ends of such compounds inaccessible is not fatal to their activity as immunostimulatory compounds.

In response, it is known in the prior art that insertion of 3'-3' linkers into a nucleotide sequence attenuates nuclease-mediated degradation as taught by Chaix. It would have been obvious to the ordinary artisan to insert such linkers

into immunomodulatory compounds in order to maintain the compounds' structural integrity. While Applicants argue that it was not known in the prior art that accessible 5' ends are crucial to the compounds' function, note that the motivation to specifically incorporate 3'-3' linkers remains and all of the structural limitations have been met by the prior art. Applicants' argument fails to provide a reason why not to use the linker while the prior art provides ample motivation to insert such a linker into a nucleotide sequence.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Double Patenting-MAINTAINED

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686

F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Deleted: ¶
Formatted: Font: Bold, Italic

Claims 42-45, 48 and 49 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 7262286 in view of Chaix. Both sets of claims are drawn to CpG-containing sequences wherein the cytidine may be modified including 5-hydroxycytosine, 5-hydromethylcytosine, N4-alkylcytosine or 4-thiouracil (see instant claims 45 and 49). U.S. Patent No. 7262286 does not teach the insertion of a 3'-3' linker within these sequences. The teachings of Chaix et al discloses that incorporating a 3'-3' linker leads to a marked increase in sequence stability compared to a sequence in the 5'-3' orientation (see Abstract) and this insertion would have been obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

Applicant's arguments filed 12/4/2008 have been fully considered but they are not persuasive. Applicant contends that part of the invention was the recognition that immunostimulatory activity requires an accessible 5' end, but not an accessible 3' end and that Applicants' invention teaches that making the 3'

ends of such compounds inaccessible is not fatal to their activity as immunostimulatory compounds.

In response, it is known in the prior art that insertion of 3'-3' linkers into a nucleotide sequence attenuates nuclease-mediated degradation as taught by Chaix. It would have been obvious to the ordinary artisan to insert such linkers into immunomodulatory compounds in order to maintain the compounds' structural integrity. While Applicants argue that it was not known in the prior art that accessible 5' ends are crucial to the compounds' function, note that the motivation to specifically incorporate 3'-3' linkers remains. Applicants' argument fails to provide a reason why not to use the linker while the prior art provides ample motivation to insert such a linker into a nucleotide sequence.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Double Patenting-NEW

Claims 20 and 41 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2 and 4 of U.S.

Patent No. 7176296 in view of Chaix. Both sets of claims are drawn to CpG-containing sequences wherein the G of this motif is a 7-deazaguanosine. U.S. Patent No. 7176296 does not teach the insertion of a 3'-3' linker within these sequences. The teachings of Chaix et al discloses that incorporating a 3'-3' linker leads to a marked increase in sequence stability compared to a sequence in the 5'-3' orientation (see Abstract) and this insertion would have been obvious to one of ordinary skill in the art at the time the invention was made.

Claims 20-21 and 41-51 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 8, 12, 13, 14 and 18-20 of U.S. Patent No. 7276489. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to an immunomodulatory sequence (or immunomer) comprising the following structural limitations: a C*pG, CpG* or C*pG*, phosphorothioates, a 3'-3' linker, two accessible 5' ends, a non-natural pyrimidine structure including 5-hydroxycytosine, 5-hydromethylcytosine, N4-alkylcytosine or 4-thiouracil, arabinose, a non-natural purine including 7-deazaguanine and phophodiester linkages.

Claims 20-21 and 41 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 7405285. Although the conflicting claims are not identical, U.S. Patent No. 7405285 claims a specific immunomer which contains the following common structural limitations to those instantly claimed: an immunostimulatory oligonucleotide containing a 3'-3' linker and a CpG motif comprising a 7-

deazaguanosine. Also, given the structures are defined as immunostimulatory, it would have been obvious to administer such compounds to a subject to induce an immune response by the ordinary artisan at the time the invention was made.

Claims 20-21 and 41 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 7427405. Although the conflicting claims are not identical, U.S. Patent No. 7427405 claims a specific immunomer which contains the following common structural limitations to those instantly claimed: an immunostimulatory oligonucleotide containing a 3'-3' linker and a CpG motif comprising a 7-deazaguanosine. Also, given the structures are defined as immunostimulatory, it would have been obvious to administer such compounds to a subject to induce an immune response by the ordinary artisan at the time the invention was made.

Claims 20-21 and 41 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 7470674. Although the conflicting claims are not identical, U.S. Patent No. 7470674 claims specific immunomers which contains the following common structural limitations to those instantly claimed: an immunostimulatory oligonucleotide containing a 3'-3' linker and a CpG motif comprising a 7-deazaguanosine. Also, given the structures are defined as immunostimulatory, it would have been obvious to administer such compounds to a subject to induce an immune response by the ordinary artisan at the time the invention was made.

Claims 20-21 and 41 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-16 of

U.S. Patent No. 7498425. Although the conflicting claims are not identical, U.S. Patent No. 7498425 claims a specific immunomer which contains the following common structural limitations to those instantly claimed: an immunostimulatory oligonucleotide containing a 3'-3' linker and a CpG motif comprising a 7-deazaguanosine. Also, given the structures are defined as immunostimulatory, it would have been obvious to administer such compounds to a subject to induce an immune response by known methods by the ordinary artisan at the time the invention was made.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHELLE HORNING whose telephone number is (571)272-9036. The examiner can normally be reached on Monday-Friday 8:00-5:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/M. H./
Examiner, Art Unit 1648

/Gary B. Nickol /
Supervisory Patent Examiner, Art Unit 1646